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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/941,438	08/28/2001	Dale P. DeVore	50063/018002	6389

21559 7590 07/07/2003

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EXAMINER
NAFF, DAVID M

ART UNIT	PAPER NUMBER
1651	7

DATE MAILED: 07/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/761,438	DeVore et al
Examiner	**Group Art Unit**
Duft	1657

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 5/18/03.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disp sition of Claims

☒ Claim(s) 1, 3-13, 15-31 + 33-36 is/are pending in the application.

Of the above claim(s)____ is/are withdrawn from consideration.

☐ Claim(s)____ is/are allowed.

☒ Claim(s) 1, 3-13, 15-31 + 33-36 is/are rejected.

☐ Claim(s)____ is/are objected to.

☐ Claim(s)____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number)____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received:____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s).____

☐ Interview Summary, PTO-413

☐ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other____

Office Action Summary

The amendment of 5/8/03 amended the specification and claims 1, 8, 13, 20, 21, 25, 26, 28-31 and 33-36, and canceled claims 2, 14 and 32.

Claims examined on the merits are 1, 3-13, 15-31 and 33-36 which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 33-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for decellularized, acylated tissue having trypsin resistance as claimed that has been acylated with an amount of acylating agent of about 0.1% to about 0.3% of wet tissue weight, does not reasonably provide enablement for decellularized tissue of the claimed trypsin resistance acylated with a different amount of acylating agent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification describes only acylated decellularized tissue with the claimed trypsin resistance that has been acylated with an amount of acylating agent as set forth above. Any amount of acylating agent would not be operable since very low amounts of acylating agent would not sufficiently disperse the tissue, and the presence of the acylating agent would not make a significant difference.

While claim 33 has been amended to recite "decellularized", the claim was not amended to recite the required amount of acylating agent.

It is suggested claim 33 be amended by after "acylated" inserting -- with about 0.1% to about 0.3% of wet tissue weight --.

Claim Rejections - 35 USC § 112

Claims 1, 8, 13, 20, 21, 25, 26 and 28-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are confusing by claims 1, 8, 13, 20, 21, 25 and 26 using percent to set forth a ratio. Ratios are not normally set forth as percentages. It is suggested that step d of claim 1 be amended by canceling "ratio" and inserting -- amount --, canceling "to wet tissue weight", and after "0.3%" inserting -- of wet tissue weight --. A corresponding amendment should be made to claims 8, 13, 20, 21, 25 and 26.

Claim Rejections - 35 USC § 102

Claims 33-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Kelman et al (5,332,802) for reasons in the previous office action of 11/08/02 and for reasons herein.

The claims are drawn to an injectable composition containing a decellularized, acylated, dispersed, dermal tissue matrix having a resistance to trypsin greater than about 40%, greater than 50%, greater than 70% or greater than 90%.

Kelman et al disclose an injectable composition (col 10, lines 55-56, and col 16, lines 53-55) containing dispersed dermal tissue (col 15, lines 9-48) that has been prepared by removing an epidermal layer,

cryopulverizing the resultant dermal tissue (col 15, lines 21, 23 and 31), and treating the tissue with succinic anhydride (col 15, line 54) as an acylating agent (col 7, line 44) to solubilize collagen of the tissue.

The dermal tissue in the composition of Kelman et al inherently has a trypsin resistance of greater than 90% as presently claimed. It is noted that the specification discloses (page 14, lines 10-20, page 15, Table 1 and page 19, Table 4) that lower amounts (about 0.16-0.20%) of acylating agent provides greater trypsin resistance. However, these results appear to be obtained when using glutaric anhydride as the acylating agent. It has not been established that the same results will be obtained when using all acylating agents within the scope of the claims. When using succinic anhydride as disclosed Kelman et al, trypsin resistance as claimed may be obtained at a higher concentration of acylating agent such as 0.5%. Additionally, Kelman et al pulverize frozen dermal tissue (col 15, lines 10-35) which is cryomilling, and the present specification discloses (page 14, lines 27-28) that cryomilling alone produces significant improvements in resistance to trypsin.

Response to Arguments

Applicants urge that in Kelman et al acylating results in complete solubilization of collagen to achieve the ability to inject the material into tissue. However, Kelman et al disclose that complete solubilizing is not required for injection. See col 10, lines 50-55, where it is recited "On the other hand, fibrillar or particulate implant material requires only partial solubilization" to obtain an injectable form. Further see col 11, lines 19-20, the recital of "completely solubilized

or the partially solubilized suspension" in regard to injectable forms. Also, see Example 2 (paragraph bridging cols 16 and 17) where partial solubilization is obtained by stopping the reaction when partial solubilization is obtained.

Applicants urge that Kelman et al does not contemplate decellularization. However, Kelman et al disclose removing noncollagenous protein contaminates (col 5, lines 41-56) and dissolving noncollagenous components in a physiological solvent (col 15, lines 19-20). Thus, it appears the process of Kelman et al results in decellularizing.

Applicants urge that Kelman et al use 60% greater acylating agent. However, the present claims do not require an amount of acylating agent. In any event, the amount of acylating agent used would depend on the acylating time and kind acylating agent used. The time of about 30 minutes to 2 hours disclosed by Kelman et al is for complete solubilizing. When not complete solubilizing as disclosed by Kelman et al as set forth above, the time would be less. As to results in Table 1 of the present specification of reduction in the amount of acylating agent increasing trypsin resistance, the acylating agent used is glutaric anhydride which is not used in the examples of Kelman et al. There inadequate evidence to establish that different acylating agents provide the same results when used for the same time and at the same concentration.

Even through Kelman et al does not mention trypsin resistance as urged by applicants, it appears partially solubilized collagen of Kelman

et al will inherently have a trypsin resistance as claimed.

Claim Rejections - 35 USC § 103

Claims 1, 3-13, 15-31 and 33-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kelman et al for reasons in the previous action.

The claims require methods and compositions involving contacting decellularized dermal or connective tissue that has been treated to reduce size and increase surface area with an acylating agent which may be in a ratio of acylating agent to wet tissue weight of about 0.1% to about 0.3%.

Kelman et al is described above.

When carrying out the process of Kelman et al of treating tissue by decellularizing, cryopulverizing and acylating, it would have required only limited routine experimentation and been obvious to select a preferred optimum amount of acylating agent to use for a particular acylating agent. Treatment of tissue as disclosed by Kelman et al (col 15, lines 10-48) will inherently decellularize the tissue. Kelman et al is using an amount of acylating agent to totally disperse and solubilize the collagen content of the tissue (col 7, lines 50-54). When less than total dispersion and solubility is sufficient, it would have been obvious to use lower amounts of the acylating agent. Moreover, there is inadequate evidence to establish that using about 0.3% provides results significantly different than when using 0.5% acylating agent as disclosed by Kelman et al when the acylating agent is that used by Kelman et al. It should be noted that "about 0.3%" encompasses an amount of acylating

agent higher than 0.3%. As to trypsin resistance, the comments set forth above apply. Using tissue other than dermal tissue such as connective tissue for treating with an acylating agent as disclosed by Kelman et al would have been a matter of individual preference depending on the function of a particular tissue desired.

Response to Arguments

Applicants arguments in regard to Kelman et al using a higher amount of acylating agent are unpersuasive since the results of using a lower amount in the present specification are when using glutaric anhydride which is not used by Kelman et al in the examples. When using succinic anhydride as disclosed by Kelman et al, an amount of acylating agent as claimed may not be adequate since different acylating agents would require different amounts for the same result. Moreover, when partially solubilizing as disclosed by Kelman et al, the amount of acylating agent can obviously be reduced, and such partially solubilized collagen will inherently have a trypsin resistance as claimed.

Claim 1, and claims dependent thereon, would be allowable if claim 1 is amended in line 1 of step d by after "agent" inserting -- for a time ranging form about 30 seconds to about 10 minutes --. Claims 13, 21, 26 and 33, and claims dependent thereon, would also be allowable if the corresponding amendment is made.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is (703) 308-0520. The examiner can normally be reached on Monday-Thursday and every other Friday from about 8:30 AM to about 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, a message can be left on voice mail.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn, can be reached at telephone number (703) 308-4743.

The fax phone number is (703) 872-9306 before final rejection or (703) 872-9307 after final rejection.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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DMN
11/5/02

DAVID M. NAFF
PRIMARY EXAMINER
ART UNIT 1651

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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DAVID M. NAFF
PRIMARY EXAMINER
ART UNIT 1651

DMN
7/3/03